

USSN: 10/729,548

Listing of the Claims

1. (original) A method of inducing quiescence in normal stem cells, the method comprising:

contacting said normal stem cells with an effective dose of a protective agent that blocks the extracellular activation of the wnt pathway in said normal stem cells;

wherein said normal stem cells rendered quiescent.

2. (original) The method according to Claim 1, wherein said stem cells comprise hematopoietic stem cells.

3. (original) The method according to Claim 2, wherein said protective agent is administered *in vivo* to a patient.

4. (original) method according to Claim 3, wherein said patient is suffering from cancer, and further comprising the step of administering to said patient an anti-proliferative agent concurrently with or following administration of said protective agent.

5. (original) The method according to Claim 4, wherein said anti-proliferative agent is selective for replicating cells.

6. (currently amended) The method according to Claim 5, —wherein said anti-proliferative agent is an anti-metabolite.

7. (original) The method according to claim 6, wherein said anti-metabolite is selected from pyrimidines, such as cytarabine (CYTOSAR-U), cytosine arabinoside, fluorouracil (5-FU), or floxuridine (FUdR); purines, such as thloguanine (6-thioguanine), mercaptopurine (6-MP), pentostatin, or fluorouracil (5-FU); or folic acid analogs, such as methotrexate, 10-propargyl-5,8-dideazafolate (PDDF, CB3717), 5,8-dideazatetrahydrofolic acid (DDATHF), or leucovorin.

8. (original) The method according to Claim 5, wherein said anti-proliferative agent is a topoisomerase inhibitor.

9. (original) The method according to Claim 8, wherein said topoisomerase inhibitor is selected from irinotecan, doxorubicin or carboplatinum.

USSN: 10/729,548

10. (original) The method according to Claim 7, further comprising the step of administering a wnt protein or wnt mimetic following said anti-proliferative agent in an amount effective to cause resumption of stem cell proliferation.

11. (original) The method according to Claim 1, wherein said protective agent binds to extracellular wnt, and inhibits the binding of said extracellular wnt to frizzled present on the surface of a stem cell.

12. (original) The method according to Claim 11, wherein said protective agent comprises at least a portion of a frizzled polypeptide.

13. (currently amended) The method according to Claim 12, wherein said protective agent comprises a frizzled cysteine rich domain (CRD) CRD fused to a plasma protein.

14. (original) The method according to Claim 13, wherein said plasma protein is a constant region of an immunoglobulin.

15. (original) The method according to Claim 11, wherein said protective agent comprises a soluble frizzled related polypeptide.

16. (withdrawn) The method according to Claim 1 wherein said protective agent comprises an immunoglobulin specific for wnt or frizzled.

17. (currently amended) A method for increasing stem cell survival in a patient to be administered a chemotherapy agent comprising the step of administering to said patient at least one protective agent that blocks extracellular wnt signaling in an amount effective to detectably inhibit the binding of extracellular wnt to frizzled present on the surface of said stem cell, wherein said protective agent is administered prior to or ~~simultaneously~~ simultaneously with said chemotherapy agent.

18. (original) A pharmaceutical composition comprising:
at least one active protective agent that blocks extracellular wnt signaling in an amount effective to detectably inhibit the binding of extracellular wnt to frizzled present on the surface of

USSN: 10/729,548

said stem cell; a chemotherapeutic agent in a dose effective for chemotherapy; and a pharmaceutically acceptable carrier.

19. (currently amended) The method according to claim 1, wherein said protective agent is selected from: ~~a soluble FZD CRD; antibodies to FZD; secreted frizzled-related proteins (sFRPs); antibodies to Wnt; antibodies LRP5/6; antibodies to Kremen; Dkk proteins; Soggy protein; Wise; fusions proteins comprising any of the above; derivatives of any of the above; variants of any of the above; and biologically active fragments of any of the above.~~

20. (currently amended) The method according to claim 19, wherein said protective agent is selected from FZD8 CRD, and FZD CRD-IgG fusion proteins, ~~SFRP-1, SFRP-2, SFRP-3, SFRP-4, SFRP-5, Dkk-1, Dkk-2, Dkk-3, Dkk-4, Soggy, Wise, antibodies to wnt 3A, antibodies to wnt 2B, antibodies to wnt 10B and antibodies to wnt 5A.~~

21. (original) A kit comprising a protective agent that blocks extracellular wnt signaling and instructions for administering to a patient said protective agent in an amount effective to detectably inhibit the binding of extracellular wnt to frizzled present on the surface of said stem cell as a therapeutic.

22. (original) The kit according to claim 21, further comprising a pharmaceutically acceptable carrier with which to admix said protective agent.

23. (original) The kit according to claim 22, further comprising means for delivery of the protective agent to a patient.

24. (original) The kit according to claim 21, further comprising a chemotherapeutic agent and instructions for administering to a patient said chemotherapeutic agent in conjunction with said protective agent in a therapeutic regime.

25. (original) The kit according to claim 21, further comprising a wnt polypeptide or a wnt mimetic and instructions for administering to a patient said wnt polypeptide or said wnt mimetic in an amount effective to competitively blocks the protective agent and allow normal stem cell proliferation to resume in a therapeutic regime.